## REMARKS/ARGUMENTS

In response to the Office Action of November 3, 2006, Applicants have amended claim 19, which when considered with the following remarks, is deemed to place the present application in condition for allowance, which action is earnestly solicited.

On page 3 of the office action, the Examiner has asked Applicants to identify whether a copy of the foreign priority papers (UK 9618952.7) were filed with the parent application since such papers could not be found. Applicants confirm that a certified copy of UK 9618952.7 was duly filed and acknowledged in great grandparent application serial no. 09/271,672 (now abandoned) which application is the grandparent application of U.S. Serial No. 10/021,117, now U.S. Patent No. 6,620,325.

Claim 19 has been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Rudat et al. (U.S. Patent No. 5,256,547). Rudat et al. has been cited for teaching a bulk quantity of cyclosporin A having an impurity level less than 0.5% by area using HPLC. As presently amended, claim 19 recites: "A bulk quantity of cyclosporin A in an amount of about 1 kg or more with an impurity level of less than 0.5% by area using HPLC."

It is respectfully submitted that presently amended claim 19 is distinguished from Rudat et al. since Rudat et al. teach only milligram and gram quantities of cyclosporin. Bulk quantities of about 1 kg or more are not taught. Accordingly, withdrawal of the rejection of claim 19 under 35 U.S.C. §102(b) is respectfully requested.

Claims 11-17, 19, 21-28, 30-36, 38-39 and 41-48 have been rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Rudat et al. (U.S. Patent No. 5,256,547). It is the Examiner's position as indicated at the top of page 5 of the office action, that based on the teaching of Rudat et al., one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Applicants respectfully traverse the rejection for the following reasons. Rudat et al. teach a fermentive production of cyclosporin A, a crude preparation by extraction,

followed by a further chromatographic purification. Such a process is not commercially feasible for obtaining bulk quantities of cyclosporin in the amount of 1 kg or more as presently claimed. Indeed, Rudat et al. teach the production of cyclosporin in the *gram* and *milligram* amounts. *See* the examples of Rudat et al., and column 6, lines 40-45, which indicate that the examples are "presented as preferred embodiments of the method of the invention." Specifically, yields obtained in Example 1 are 1100 mg cyclosporin A per liter with no purity data given. The lack of purity data is presumably because the 1100 mg of cyclosporin A is obtained after fermentation and extraction, and before further chromatographic purification. Example 2 provides a yield of 1150 mg Cyclosporin A per liter with no purity data given for the same reasons. Example 3 indicates a yield of Cyclosporin A of "a maximum of 3150 mg/liter", no purity data given. Example 5 provides a yield of 5.2 g of almost white product with 99% by mass Cyclosporin A according to HPLC analysis. Example 6 provides a yield of 102 grams, content (HPLC) **97.5%** cyclosporin A. Example 7 provides a mycelia-Precosite mixture with an active ingredient of 6.3 g/kg of mixture. Example 8 provides a further purification of the product of Example 7, and gives a yield of 6.1 g of "pure" Cyclosporin A. No quantitative purity level is provided in this example.

In contrast, the presently pending claims and presently amended claim 19 recite in relevant part: "A bulk quantity of cyclosporin in an amount of about 1 kg or more..." All of the presently pending claims and presently amended claim 19 also require the cyclosporin to have a purity level of 99.5% or greater. Page 11 of the present application, under "Commercial scale" indicates that 50 kg of cyclosporin is produced having a purity of at least 99.5% by weight. Page 12, second paragraph, indicates that a bulk quantity of 100 kg cyclosporin A is produced having a purity of at least 99.5% by weight. These quantities produced by Applicants are *orders of magnitude higher* than the quantities of cyclosporin produced by Rudat et al. Example 6 of Rudat et al. produce a tenth of the lower level of bulk quantity presently claimed by Applicants. Example 6 however, only has a purity level of 97.5%.

Applicants respectfully submit that the presently claimed invention would not have been considered obvious since one skilled in the art having Rudat et al. in hand would not have reasonably expected to produce bulk quantities of about 1 kg or more of cyclosporin following the teachings provided therein. As described above, Rudat et al.

produce orders of magnitude lower yields than Applicants or else produce a tenth of the lower limit of yield presently claimed by Applicants but with a lower purity level presently claimed by Applicants.

Applicants respectfully submit that it was only after developing a counter current extraction process as disclosed in the present application, that bulk quantities of cyclosporin with such high purity levels could be obtained. Since Rudat et al. fails to suggest either the presently claimed product or the process of making the product, claims 11-17, 19, 21-28, 30-36 38-39 and 41-48 are non-obvious over Rudat et al. Withdrawal of the rejection of these claims under 35 U.S.C. §103(a) is therefore warranted.

In view of the foregoing remarks and amendments, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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